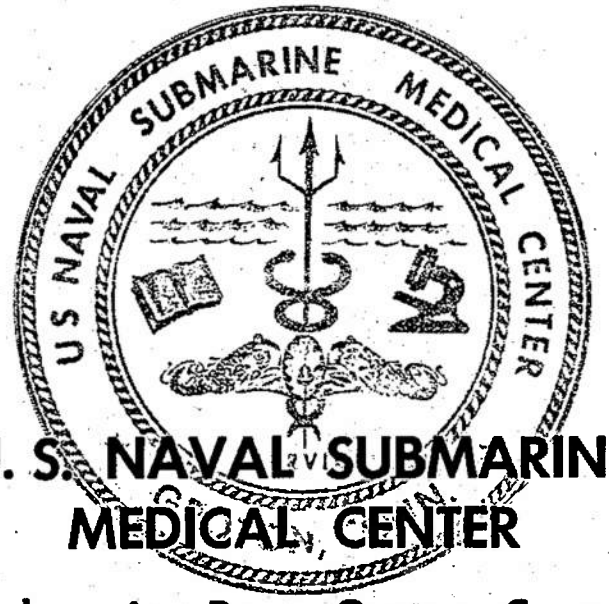

U. S. NAVAL SUBMARINE MEDICAL CENTER

Submarine Base, Groton, Conn.

REPORT NUMBER 668

HYPERBARIC AIR AND CORNEAL VASCULARIZATION

by

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Bureau of Medicine and Surgery, Navy Department
Research Work Unit MR011.01-5012

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24 June 1971

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NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY
NAVAL SUBMARINE MEDICAL CENTER REPORT NUMBER 668

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SUMMARY PAGE

THE PROBLEM

To determine whether oxygen-lack might be one of the basic causes of corneal vascularization following injury.

FINDINGS

Exposure of rabbit corneas to hyperbaric air for continuous periods of up to two weeks to increase oxygen content of the corneal tissue showed no effect on the neovascularization following experimental burns of the cornea. These results confirm and extend the results obtained by previous investigators.

APPLICATIONS

This useful, even though negative, information in the Navy's quest for possible use of hyperbaric air in the treatment of burns of the cornea, should be of interest to other research scientists working in this field.

ADMINISTRATIVE INFORMATION

This investigation was conducted as a pilot study under independent work unit MR011.01-5012 to determine whether hyperbaric air might hold promise of being valuable in treatment of eye burns. The manuscript was approved for publication on 24 June 1971 and designated as NavMedRschLab Report No. 668.

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ABSTRACT

Hypoxia is one of the factors postulated as promoting vascularization of the cornea. However, previous experiments designed to increase tissue oxygen for short or intermittent periods have had no effect in retarding neovascularization. The present study utilized rabbit exposure to hyperbaric air for continuous periods of up to two weeks to increase tissue oxygen, and demonstrated no effect on the neovascularization caused by sodium hydroxide burns of the cornea. This confirms previous experimental results and tends to rule out inadequate time periods or intermittency of exposure as factors in previous negative results.

HYPERBARIC AIR AND CORNEAL VASCULARIZATION

INTRODUCTION

Studies on the possible basic causes of corneal vascularization have been reported by many investigators,[1-9] but no consistent set of conditions has been established to explain the phenomenon. One of the many possible factors suggested has been a relative hypoxia of the cornea,[10-13] and several researchers have evaluated the effect of increasing the concentration alone,[14,15] or both the pressure and concentration of oxygen[16,17] to which experimental animals were exposed. The present study differs from previous ones in that the experimental animals were exposed primarily to hyperbaric air, rather than 50-100% oxygen, for continuous periods of up to two weeks immediately following chemical injury. This has the effect of providing increased oxygen tension without altering the percentage relationships (20% oxygen) of normal air components, and the experimental animals seem to tolerate this better for longer periods of time than if the oxygen percentage is also increased. The treatment period of approximately two weeks is a much longer period of continuous exposure to increased oxygen tension than has previously been reported.

MATERIALS AND METHODS

Adult male chinchilla rabbits weighing approximately 5 kg. were used for test and control subjects. A large spherical 2,000 foot equivalent sea water pressure hyperbaric chamber was used for all tests. Pressure, temperature, O_2 and CO_2 content of chamber gases were monitored at all times. Lithium hydroxide was used for CO_2 scrubbing. The chamber was pressurized to test depth at the rate of 75 feet (sea water equivalent) per minute and depressurized at 33 feet per minute.

Four rabbits were used in the first experiment and ten rabbits were used in experiments two and three. After topical anesthesia, corneal lesions were produced with a three millimeter glass rod which had been dipped in a 20% NaOH solution and then applied to the superior cornea approximately four millimeters from the limbus. This produced an immediate opacity with a clear area of two to three millimeters between the lesion and the limbus in most animals. Half the animals were returned to their cages and the other half placed immediately in the hyperbaric chamber and pressurized. Water and food were available to both groups on demand.

In all three experiments, room air at a pressure of three atmospheres were used. The only variant was in the third experiment where eleven evenly spaced two-hour periods of O_2 concentration increased to 90-95% (PO_2 2166 $\pm$ 12 millimeters Hg.) were used. Control animals were examined daily to evaluate the progression and character of the neovascularization. With the exception of those which expired prematurely, test animals were not examined until the end of the experiment in order not to break the continuity of increased oxygen tension. At the end of the test period, both test and control animal

eyes were photographed, the extent of corneal vascularization measured, and the density of vessel growth noted as light, medium, or heavy. The eyes were then enucleated and fixed in formalin for later histopathologic study.

RESULTS

Corneal vascularization was noted in the control animal eyes four to five days after the corneal burn. Vessel growth in both length and number increased during the next ten days to a maximum of 3 1/2 millimeters in some of the control and test animals, with a minimum of 1 1/2 millimeters and an average of 2.7 millimeters. Maximum vessel growth occurred between the sixth and tenth days following injury in the control animals. Density of the vessels was variable, but did not seem to be related to differences in air pressure.

Table I is a summary of the final results and indicates no significant difference between test and control eyes in the extent of corneal vascularization. If anything, there was slightly greater vascularization in the eyes exposed to increased pressure, but this is by no means statistically significant. It should be noted that several test animals in experiments two and three died during the period of increased pressure, apparently in respiratory distress secondary to pulmonary edema. These eyes were not included in the tabulated results, however, the extent and nature of vessel growth was noted to be comparable to that of the control animals at the same stage. Figure #1 illustrates the typical lesion and pattern of vessel growth seen in both test and control animals after eleven days.

TABLE I

Exp. No.	Length of Experiment (Days)	No. of Eyes		No. of Eyes in Surviving Animals		Average Length Vessels		Air Pressure
		Test	Control	Test	Control	Test	Control	
1	12	4	4	4	4	2.5	2.3	3 atm
2	14	10	10	4	10	2.5	2.5	3 atm
3	11	10	10	2	8	3.5	2.8	*3 atm
Totals	12.3 av	24	24	10	22	2.7	2.6 av	

*Periods of increased O_2 percentage during experiment.

Fig. 1. Pattern of vascularization typical of both cornea and test eyes 11 days following injury.

COMMENT

All previous studies concerning the effect of increased oxygen percentage or pressure on neovascularization of the cornea have been negative.[14-17] Our results are also negative, indicating that even prolonged continuous exposure to increased oxygen tension does not inhibit the corneal vascularization caused by alkali burns.

Intermittency or unduly short periods of exposure are thus ruled out as factors in the failure of increased oxygen tension to retard vascularization. This tends to confirm the evidence from other investigators that a relative state of hypoxia in itself is not a significant factor in causing vascular proliferation in the cornea.

Two chief possibilities remain to explain the absence of any effect by hyperbaric air. (1) The oxygen tension level was too low to have any effect even over a prolonged period of time. (2) The increased level actually has a deleterious effect on aerobic metabolism, as suggested previously by Lazar et al[17] from evidence published by Haugaard.[18] The first possibility would be difficult to

prove or disprove in vivo because of the systemic toxicity of high levels of oxygen. The second possibility could explain the greater vessel growth observed in some of our hyperbaric animals as compared to controls and could still be compatible with other good experimental evidence that hypoxia under certain conditions can stimulate vessel growth. *5, 10, 13*

The fact remains that to date there is no evidence that increased tissue oxygen has any effect in retarding neovascularization in experimental corneal injury.

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Neovascularization						
Oxygen tension						